(b) introducing the conjugated peptide nucleic acid of step (a) into liposomes; and

(c) contacting the product of step (b) with a cell.

REMARKS

Claims 21, 23-27, 31-34, 38-41, 45-48, and 52 are pending.

Claims 23, 25-27, and 31 stand rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by PCT Patent Application WO/92/20702 ("the 702 Application"). Applicants request reconsideration of this rejection because the 702 Application does not actually describe any claimed invention in a way that would place it in the possession of those skilled in the art. *In re Arkley*, 172 U.S.P.Q. 524, 528 (CCPA 1972) ("The test which determines whether an invention has been anticipated by a reference is whether the description of the invention in the reference is sufficient to put the public in possession of the invention.") Since the structures recited in claims 23, 24, and 25 do not appear in the 702 Application, Applicants surmise that the instant rejection has been entered because the Examiner is of the view that one skilled in the art could have produced a claimed invention by picking and choosing from among the many variables presented on pages 8-10 of the 702 Application. However, the need for such picking and choosing is plainly inconsistent with a finding of anticipation. *Id.*, 172 U.S.P.Q. at 526; *In re Schaumann*, 572 F.2d 312, 314 (C.C.P.A. 1978) ("By having to select [a variable] from among the many possibilities which R in the structural formula [of the reference] may be, . . . does not give rise to the claimed compound being fully anticipated by the reference."). Given the unduly generic nature of the 702 Application's disclosure, the rejection for alleged anticipation is improper and should be withdrawn.

Claims 21, 23-27, 31-34, and 38 stand rejected under 35 U.S.C. § 103 as allegedly being obvious in view of the combined teaching of the 702 Application and Renneisen, *et al*, *Journal of Biological Chemistry*, **1990**, 265, 16337-16342 ("the Renneisen reference"). Applicants request reconsideration of this rejection because the Office Action fails to identify any reason why those of ordinary skill in the art would have been motivated to combine the references' teachings in the manner the Office Action proposes.

Although the Office Action appears to allege that a person of ordinary skill could have produced one of the recited compounds by picking and choosing from among the many variables presented on pages 8-10 of the 702 Application, the Office Action fails to identify any reason why such a person would have actually been motivated to do this. Indeed, the picking and choosing that would have been necessary in this sort of undertaking would have been considerable, requiring selection from, for example, the C, B, A, D, G Q, I and R possibilities of Structure I presented on pages 8-10. The Office Action does not identify any motivation to make the choices that would lead to a claimed compound, as opposed to the choices that would lead to the many other compounds that conceivably are within the ambit of the 702 Application's disclosure. Accordingly, the rejection for alleged obviousness in view of the 702 Application is improper and should be withdrawn. *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1458 (Fed. Cir. 1998). ("the examiner must show reasons that the skilled artisan, confronted with the same problem as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed."); *In re Baird*, 16 F.3d 380, 382, 29 U.S.P.Q.2d 1550, 1552 (Fed. Cir. 1994) ("The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious.").

To the extent that the 702 Application has been combined with the Renneisen reference, such a combination is untenable. As the Office Action admits (April 3, 2002 Office Action at page 3), the 702 Application contains no suggestion that liposomes are useful carriers for the instant invention. The Renneisen reference shows only encapsulation of antisense *RNA* into certain liposomes. The Rennesien reference does not show use of *peptide nucleic acids* (PNAs). Finding no suggestion to combine the references, it appears that the Examiner has improperly used the Applicant's disclosure as a guide instead of factual evidence. *In re Fritch*, 23 U.S.P.Q.2d 1780, 1784 (Fed. Cir. 1992) ("it is impermissible for an Examiner, in proffering a 35 U.S.C. § 103 rejection, to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art to render the claimed invention obvious."). Thus, it is respectfully submitted that neither the 702 Application nor the Renneisen reference teach or suggest modifying the teachings of the 702 Application in a way that would

provideany of Applicant's claimed inventions. The rejection under §103 should therefore be withdrawn.

Claims 39-41, 45-48, and 52 stand rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement with respect to the recited methods. The instant specification, however, provides considerable disclosure relating to these methods, and there is no evidence of record refuting Applicants' assertion that those skilled in the art would be able to practice the claimed methods to at least some measurable extent. The specification, for example, teaches sites and modes of administration, dose level and administration regimen, and the nature of the pharmaceutical composition (page 15, line 31 to page 18, line 20 of the instant specification). That some experimentation may be required to determine optimum parameters does not preclude enablement so long as the amount of experimentation is not unduly extensive. *W. L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 U.S.P.Q. 303, 316 (Fed. Cir. 1983).

Despite Applicants' considerable disclosure, the Office Action asserts that enablement is lacking because the claimed compounds might be inefficiently taken up by cells. However, since there is no evidence suggesting that the claimed compounds will not be taken up to at least some measurable extent, it is not seen how the potential for inefficient uptake is relevant in assessing enablement of the claimed inventions. The Office Action also alleges difficulty in correlating experiments conducted with cultured cells with results obtained in whole organisms (August 2, 2000 Office Action at page 22). The rejection appears to be predicated on the subjective belief that therapeutic data is required to "adequately teach" that effect. The patent laws, however, do not require such data. The first paragraph of Section 112, for example, requires nothing more than objective enablement. The particular means through which an applicant chooses to enable the practice of his invention, either by the use of illustrative examples or by broad terminology, is of no importance. *In re Marzocchi and Horton*, 169 U.S.P.Q. 367 (C.C.P.A. 1971) (emphasis added).

When the present specification is judged in light of the proper test for enablement, it is clear that Applicant has provided extensive teachings as to how to make and how to

use the claimed compounds. As such, Applicants respectfully submit that the rejection should be withdrawn.

The amendment of claim 21 is believed to render the rejection under 35 U.S.C. §112, second paragraph is moot. The basis for the amendment can be found, for example, at page 11, lines 4-25 of the originally filed specification.

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. Accordingly, an early and favorable reconsideration of the rejections and an allowance of all of pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 15-18, and 20 have been canceled.

Claim 21 is amended as follows:

21. A method of modulating cellular uptake and distribution of a peptide nucleic acid comprising the steps of:

(a) conjugating said peptide nucleic acid with a group selected from alkyl, lipid, and steroid; [and]

(b) introducing the conjugated peptide nucleic acid of step (a) into liposomes; and

(c) contacting the product of step (b) with a cell.